

MAERTENS et al.  
Serial No. 09/638,693  
June 24, 2003

**IN THE CLAIMS**

Amend the claims as follows.

Claims 1-55 (Canceled).

147  
56. (Currently Amended) An isolated polypeptide or peptide ~~consisting~~  
of comprising 5 or more contiguous amino acids selected from at least one HCV  
polypeptide or peptide selected from the group consisting of:

an HCV type 3a polypeptide or peptide selected from the region spanning  
positions 140 to 319 of the Core/E1 region of HCV type 3a;

an HCV type 3a polypeptide or peptide selected from the region spanning  
positions 1556 to 1650 of the NS3/NS4 region of HCV type 3a;

an HCV type 3a polypeptide or peptide selected from the region spanning  
positions ~~1664~~1646 to 1764 of the NS3/NS4 region of HCV type 3a;

an HCV type 4 polypeptide or peptide selected from the region spanning  
positions 127 to 319 of the Core/E1 region of HCV type 4;

an HCV type 4 polypeptide or peptide selected from the region spanning  
positions 192 to 319 of the E1 region of HCV type 4;

an HCV type 4 polypeptide or peptide selected from the region spanning  
positions 2645 to 2757 of the NS5B region of HCV type 4;

an HCV type 5 polypeptide or peptide selected from the region spanning  
positions 1 to 191 of the Core region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning  
positions 192 to 319 of the E1 region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning  
positions 1 to 319 of the Core/E1 region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions ~~328 to 546~~308 to 503 of the E1/E2 region of HCV type 5;

an HCV subtype 5 polypeptide or peptide selected from the region spanning positions 1286 to 1403 of the NS3 region of HCV subtype 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 1646 to 1764 of the NS3/NS4 region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 1284 to 1764 of the NS3/NS4 region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 2645 to 2757 of the NS5 region of HCV type 5;

an HCV subtype 2d polypeptide or peptide selected from the region spanning positions 1 to 319 of the Core/E1 region of HCV subtype 2d;

an HCV subtype 2d polypeptide or peptide selected from the region spanning positions 192 to 319 of the E1 region of HCV subtype 2d;

an HCV subtype 2d polypeptide or peptide selected from the region spanning positions 2645 to 2757 of the NS5B region of HCV subtype 2d;

wherein said peptide or polypeptide contains at least one genotype-specific amino acid.

57. (Previously Amended) An HCV type 5 polypeptide or peptide selected from the region spanning positions 1 to 2757 of HCV type 5, and wherein said peptide or polypeptide is obtainable by amplification of HCV type 5 specific polynucleic acids using HCV type 5 specific primers,

and wherein said peptide or polypeptide contains at least one genotype-specific amino acid.

58. (Currently Amended) An isolated HCV type 3a polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 14, 16, 18, 20, 22, or 24, 26  
or 28,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 140 to 319 of the Core/E1 region of HCV type 3a.

59. (Currently Amended) An isolated HCV type 3a polypeptide comprising an amino acid sequence or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 30, 32, 34, 36, 38, or 40  
or 223,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1646 to 1764 of the NS3/NS4 region of HCV type 3a.

60. (Currently Amended) An isolated HCV type 4 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 419, 421 or 123,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 127 to ~~349~~ 317 of the Core/E1 region of HCV type 4.

61. (new) An isolated HCV type 4 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: ~~119, 121 or 123,~~ 168, 170, 172, 174, 176, 178, 180, 182, 186, 188 or 190

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 192 to 319 of the E1 region of HCV type 4.

62. (Currently Amended) An isolated HCV type 4 polypeptide or peptide selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 107, 109, 111, 113, 115-~~or~~, 117, 202, 204, 208, 210 or 212,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 2645 to 2757 of the NS5B region of HCV type 4.

47  
63. (Currently Amended) An isolated HCV type 4 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 164 or 194-~~166,~~

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to ~~349~~166 of the Core/E1 region of HCV type 4.

64. (Currently Amended) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: ~~42, 44, 46, 48, 50, or 52, 54,~~  
~~or 152,~~

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 191 of the Core region of HCV type 5.

65. (Currently Amended) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: ~~42, 44, 46, 48, 50, 52, 152, or~~  
~~156 or 54,~~

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 192 to 319 of the E1 region of HCV type 5.

66. (Currently Amended) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: ~~42, 44, 46, 48, 50, or 52, 54, 154 or 156,~~

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 319 of the Core/E1 region of HCV type 5.

67. (Currently Amended) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptide or peptide of SEQ ID NO: 158,  
(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions ~~328 to 546~~ 308 to 503 of the ~~Core/E1~~ E1/E2 region of HCV type 5.

68. (Currently Amended) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 56, or 58,  
(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1286 to 1403 of the NS3 region of HCV type 5.

69. (Currently Amended) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 60, or 62,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1646 to 1746 of the NS3/NS4 region of HCV type 5.

70. (Currently Amended) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 160 or 162,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 2645 to 2757 of the NS5 region of HCV type 5.

71. (Currently Amended) An isolated HCV subtype 2d polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 144,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 319 of the Core/E1 region of HCV subtype 2d.

72. (Currently Amended) An isolated HCV subtype 2d polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptide or peptide of SEQ ID NO: 144,

H7

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 192 to 319 of the E1 region of HCV subtype 2d.

73. (Currently Amended) An isolated HCV subtype 2d polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptide or peptide of SEQ ID NO: 146,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 2645 to 2757 of the NS5B region of HCV subtype 2d.

74. (Currently Amended) An isolated HCV polypeptide or peptide according to any of claims 56 or 57, which contains in its sequence at least one of the following amino acid residues:

L7, M44, R67, Q70, A79, A87, N106, K115, A127, A190, S130, V134, G142, I144, E152, A157, V158, P165, S177 or Y177, I178, V180 or E180 or ~~F182~~, R184, I186, H187, T189, A190, S191 or ~~G191~~, Q192 or ~~L192~~ or I192 or ~~V192~~ or E192, N193 or H193 or P193, W194 or ~~Y194~~, H195, A197 or ~~I197~~ or ~~V197~~ or ~~T197~~, ~~V202~~, ~~I203~~ or ~~L203~~, Q208, A210, V212, F214, ~~T216~~, R217 or D217 or ~~E217~~ or V217, H218 or N218, H219 or ~~V219~~ or L219, L227 or I227, M231 or E231 or Q231, ~~T232~~ or ~~D232~~ or A232 or K232, ~~Q235~~ or I235, A237 or T237, I242, I246, S247, S248, V249, S250 or ~~Y250~~, I251 or V251 or M251 or F251, D252, ~~T254~~ or V254, L255 or V255, E256 or ~~A256~~, M258 or F258 or V258, ~~A260~~ or Q260 or S260, A261, T264 or Y264, M265, I266 or A266, A267,

G268 or T268, F271 or M271 or ~~V271~~, I277, M280 or H280, ~~I284~~ or A284 or ~~L284~~,  
V274, ~~V291~~, N292 or S292, ~~R293~~ or I293 or Y293, Q294 or ~~R294~~, L297 or I297 or  
Q297, A299 or K299 or Q299, N303 or ~~T303~~, T308 or L308, T310 or F310 or A310 or  
D310 or V310, L313, G317 or Q317, L333, S351, A358, A359, A363, S364, A366,  
T369, L373, F376, Q386, I387, S392, I399, F402, I403, R405, D454, A461, A463, T464,  
K484, Q500, E501, S521, K522, H524, N528, S531, S532, V534, F536, ~~F537~~, M539,  
I546, ~~C1282~~, ~~A1283~~, H1310, V1312, Q1321, P1368, ~~V1372~~, V1373, K1405, Q1406,  
~~S1409~~, A1424, A1429, C1435, S1436, S1456, H1496, A1504, D1510, D1529, I1543,  
N1567, D1556, N1567, M1572, Q1579, L1581, S1583, F1585, V1595, E1606 or T1606,  
M1611, V1612 or L1612, P1630, C1636, ~~P1651~~, T1656 or I1656, L1663, V1667, V1677,  
A1681, H1685, E1687, G1689, V1695, A1700, Q1704, Y1705, A1713, A1714 or S1714,  
M1718, D1719, A1721 or T1721, R1722, A1723 or V1723, H1726 or G1726, E1730,  
V1732, F1735, I1736, S1737, R1738, T1739, G1740, Q1741, K1742, Q1743, A1744,  
T1745, L1746, E1747 or K1747, I1749, A1750, T1751 or A1751, V1753, N1755, K1756,  
A1757, P1758, A1759, H1762, T1763, Y1764, P2645, A2647, K2650, K2653 or L2653,  
S2664, N2673, F2680, K2681, L2686, ~~H2692~~, Q2695 or L2695 or I2695, V2712, F2715,  
V2719 or Q2719, T2722, T2724, S2725, R2726, G2729, Y2735, H2739, G2746 or  
I2746, I2748, P2752 or K2752, P2754 or T2754, T2757 or P2757.

75. (Currently Amended) A polypeptide or peptide according to any of claims 56  
or 57, wherein said polypeptide or peptide is selected from the following peptides:

QPTGRSWGQ (SEQ ID NO 93)

RSEGRTSWAQ (SEQ ID NO 220)

RTEGRTSWAQ	(SEQ ID NO 221)
LEWRNTSGLYVL	(SEQ ID NO 83)
VNYRNASGIYHI	(SEQ ID NO 126)
QHYRNISGIYHV	(SEQ ID NO 127)
EHYRNASGIYHI	(SEQ ID NO 128)
IHYRNASGIYHI	(SEQ ID NO 224)
VPYRNASGIYHV	(SEQ ID NO 84)
VNYRNASGIYHI	(SEQ ID NO 225)
VNYRNASGVYHI	(SEQ ID NO 226)
<del>VNYHNTSGIYHL</del>	<del>(SEQ ID NO 227)</del>
QHYRNASGIYHV	(SEQ ID NO 228)
QHYRNVSGIYHV	(SEQ ID NO 229)
IHYRNASDGYI	(SEQ ID NO 230)
LQVKNTSSSYMV	(SEQ ID NO 231)
VYEADDVILHT	(SEQ ID NO 85)
VYETEHILHL	(SEQ ID NO 129)
VYEADHHIMHL	(SEQ ID NO 130)
VYETDHHILHL	(SEQ ID NO 131)
VYEADNLILHA	(SEQ ID NO 86)
<del>VWQLRAIVLHV</del>	<del>(SEQ ID NO 232)</del>
VYEADYHILHL	(SEQ ID NO 233)
VYETDNHILHL	(SEQ ID NO 234)
VYETENHILHL	(SEQ ID NO 235)

49

VFETVHH1LHL ~~————— (SEQ ID NO 236)~~  
VFETEHHILHL ~~————— (SEQ ID NO 237)~~  
VFETDHHIMHL (SEQ ID NO 238)  
VYETENHILHL (SEQ ID NO 239)  
VYEADALILHA ~~————— (SEQ ID NO 240)~~  
VQDGNTSTCWTPV (SEQ ID NO 87)  
VQDGNTSACWTPV (SEQ ID NO 241)  
VRVGNQSRCWVAL (SEQ ID NO 132)  
VRTGNTSRCWVPL (SEQ ID NO 133)  
VRAGNVSRCWTPV (SEQ ID NO 134)  
EEKGNISRCWIPV (SEQ ID NO 242)  
VKTGNQSRCWVAL (SEQ ID NO 243)  
VRTGNQSRCWVAL (SEQ ID NO 244)  
~~VKTGNQSRCWIAL ————— (SEQ ID NO 245)~~  
~~VKTGNVSRWCWPL ————— (SEQ ID NO 247)~~  
VKTGNVSRCWISL (SEQ ID NO 248)  
VRKDNVSRCWVQI (SEQ ID NO 249)  
VRYVGATTAS (SEQ ID NO 89)  
APYIGAPLES (SEQ ID NO 135)  
APYVGAPLES (SEQ ID NO 136)  
AVSMDAPLES (SEQ ID NO 137)  
APSLGAVTAP (SEQ ID NO 90)  
APSFHAVTAP (SEQ ID NO 250)

VSQPGALTKG	(SEQ ID NO 251)
VKYVGATTAS	(SEQ ID NO 252)
APYIGAPVES	(SEQ ID NO 253)
AQHLNAPLES	(SEQ ID NO 254)
SPYVGAPLEP	(SEQ ID NO 255)
SPYAGAPLEP	(SEQ ID NO 256)
APYLGAPLEP	(SEQ ID NO 257)
APYLGAPLES	(SEQ ID NO 258)
APYVGAPLES	(SEQ ID NO 259)
VPYLGAPLTS	(SEQ ID NO 260)
APHLRAPLSS	(SEQ ID NO 261)
APYLGAPLTS	(SEQ ID NO 262)
RPRRHQTVQT	(SEQ ID NO 91)
QPRRHWTQD	(SEQ ID NO 138)
RPRRHWTQD	(SEQ ID NO 139)
RPRQHATVQN	(SEQ ID NO 92)
RPRQHATVQD	(SEQ ID NO 263)
SPQH HKFVQD	(SEQ ID NO 264)
<del>RPRRLWTTQE</del>	<del>(SEQ ID NO 265)</del>
<del>PPRIHETTQD</del>	<del>(SEQ ID NO 266)</del>
<del>TISYANGSGPSDDK</del>	<del>(SEQ ID NO 267)</del>

H7

76. (Previously Added) A composition comprising an isolated polypeptide or peptide according to any of claims 56 or 57.

77. (Previously Added) A method for raising antibodies comprising the use of a polypeptide or peptide according to any of claims 56 or 57.

78. (Previously Added) A method of detecting, screening or confirmation for the presence of HCV antibodies present in a biological sample, comprising the following steps:

- (i) providing a sample suspected of containing HCV antibody,
- (ii) contacting the sample with a polypeptide or peptide according to any of claims 56 or 57, under appropriate conditions allowing the formation of an immune complex,
- (iii) inferring from the presence of the immune complex of step (ii) the presence of HCV antibodies in said sample.

79. (Previously Added) A method of detecting, screening or confirmation for one or more HCV serotypes present in a biological sample, comprising the following steps:

- (i) providing a sample suspected of containing HCV antibody,
- (ii) contacting the sample with a polypeptide or peptide according to any of claims 56 or 57, under appropriate conditions allowing the formation of an immune complex,

H7

(iii) inferring from the presence of one or more of these immune complexes of step (ii) the serotype(s) present in said sample.

80. (Previously Added) A method for detecting HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following steps:

(i) contacting the biological sample to be analyzed for the presence of HCV antibodies with at least one peptide or polypeptide according to any of claims 56 or 57, preferentially in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide or peptide is preferentially in the form of a biotinylated polypeptide or peptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes,

(ii) removing unbound components,

(iii) incubating the immune complexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,

(iv) detecting the presence of said immune complexes visually or by means of densitometry and inferring the HCV serotype(s) present from the observed binding pattern.

47 81. (Previously Amended) A method for confirmation of HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following steps:

(i) contacting the biological sample to be analyzed for the presence of HCV antibodies with at least one peptide or polypeptide according to any of claims 56 or 57, preferentially in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide or peptide is preferentially in the form of a biotinylated polypeptide or peptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes,

(ii) removing unbound components,

(iii) incubating the immune complexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,

(iv) detecting the presence of said immune complexes visually or by means of densitometry and confirm the HCV serotype(s) present from the observed binding pattern.

82. (Previously Added) A kit for detecting, screening or confirmation for one or more HCV serotype(s) present in a biological sample, comprising:

(i) a polypeptide or peptide according to any of claims 56 or 57,  
(ii) possibly a buffer and components necessary for producing the formation of an immune complex,

H7  
(iii) possibly a means for detecting, screening or confirming the immune complex(es) formed.

83. (Previously Amended) A kit for detecting, screening or confirmation for the presence of HCV antibodies present in a biological sample, comprising the following steps:

- (i) a polypeptide or peptide according to any of claims 56 or 57,
- (ii) possibly a buffer and components necessary for producing the formation of an immune complex,
- (iii) possibly a means for detecting, screening or confirming the immune complex formed.

84. (Previously Amended) A kit for detecting HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following components:

- (i) at least a polypeptide or peptide according to any of claims 56 or 57, with said polypeptide or peptide being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
- (ii) a buffer and components necessary for producing the buffer enabling binding reaction between these polypeptides or peptides and the antibodies against HCV present in the biological sample,
- (iii) optionally, a detector for determining the presence of immune complexes formed in the preceding binding reaction, and
- (iv) optionally an automated scanning and interpretation device to confirm the HCV serotype(s) present in the sample from the observed binding pattern.

H7

85. (Previously Amended) A kit for confirmation of HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following components:

- (i) at least a polypeptide or peptide according to any of claims 56 or 57, with said polypeptide or peptide being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,
- (ii) a buffer and components necessary for producing the buffer enabling binding reaction between these polypeptides or peptides and the antibodies against HCV present in the biological sample,
- (iii) optionally, a detector for determining the presence of immune complexes formed in the preceding binding reaction, and
- (iv) optionally, an automated scanning and interpretation device to confirm the HCV serotype(s) present in the sample from the observed binding pattern.

86. (new) An isolated HCV type 3a polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptide or peptide of SEQ ID NO: 30,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1556 to 1650 of the NS3/NS4 region of HCV type 3a.

87. (new) An isolated HCV type 4 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 168, 170, 172, 174, 176, 178, 180, 182, 186, 188, or 190

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 127 to 319 of the Core/E1 region of HCV type 4.

88. (new) An isolated HCV type 4 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 166,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 126 of the Core region of HCV type 4.

89. (new) An isolated HCV type 4 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 192,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 96 of the Core region of HCV type 4.

90. (new) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 156,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 127 to 319 of the Core/E1 region of HCV type 5.

91. (new) An isolated HCV type 5 polypeptide or peptide comprising an amino acid sequence selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 198, 200, or 270,
  - (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1284 to 1764 of the NS3/NS4 region of HCV type 5.
- 

117  
Coul